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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/913,402	08/14/2001	Tsuneyuki Nagae	PO7336US00/LRP	8312

881 7590 06/21/2007

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EXAMINER	
CHONG, YONG SOO	
ART UNIT	**PAPER NUMBER**
1617	

MAIL DATE	DELIVERY MODE
06/21/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/913,402	NAGAE ET AL.	
	Examiner	Art Unit	
	Yong S. Chong	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/30/2007 has been entered.

Claim(s) 1-2 have been cancelled. Claim(s) 5-6 have been added. Claim(s) 3-6 are pending and examined herein.

Applicant's arguments have been fully considered but found not persuasive. The rejection(s) of the last Office Action are maintained for reasons of record and modified below as a result of the new claim amendments.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham vs John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 3-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nyamekye et al. (Circulation 1995; 91:417-425) in view of Narciso Jr., (US Patent 5,298,018), Aizaw et al. (US Patent 5,308,861), and Antoshkiw et al. (US Patent 4,471,779).

The scope of the pending claims is essentially directed to a method of performing photodynamic therapy to reduce restenosis post an angioplasty procedure comprising administering Npe6 intravenously to a patient who has undergone an angioplasty procedure and subjecting the patient at a point of 0.5-6 hours after administration of Npe6 to a local irradiation of laser light of 664 nm wavelength at laser fluence of 1-10 J/cm2. Examiner adds that the delivery process instantly described in claim 3 is inherent to the PCTA procedure and those described by the cited prior art.

For example, Narciso teaches that photodynamic therapy during PCTA procedure to limit restenosis of a blood vessel intima subject to a smooth cell proliferation (see abstract). Narciso specifically explains that the use of a photodynamic agent can be during, before or after a PCTA procedure (see col 2, lines 6-65). Narciso also suggests Npe6 to be a suitable photosensitizer for such treatment (see col 7, table 1, under class Phorobides). Since Narciso teaches the use of photodynamic therapy during a PCTA procedure, all method steps of the instant claims are also inherently disclosed.

Nyamekye teaches methods of administering photodynamic therapy to a mammal for inhibiting the development of intimal hyperplasia (restenosis) caused by a vascular intervention procedure such as balloon angioplasty (see abstract; pages 3-5). Nyamekye clearly teaches inhibiting restenosis in vessels of rats that have undergone a balloon angioplasty and have experienced stretch injury of arorta. (see page 8-9). Such teaching meets the instant limitation of suppressing thickening of vascular intima of blood vessels.

Nyamekeye uses 5-amiono-levulinic acid as the photosensitizer and applies a laser radiation of about 50 J/cm2 at 630 nm wavelength for a period of 30-90 minutes after administration of the photosensitizer (see page 3-5, under the heading "methods and material"). Nyamekyes administers his photodynamic methodology to rats after they have undergone an angioplasty procedure. Nyamekyes suggests photodynamic therapy given at suitable time after angioplasty will eliminate the expected restenosis post an angioplasty procedure (see page 13, last para). Nyamekye fails to explicitly teach the use of mono-L-aspartylch!orin e6 at a laser wavelength of 667 nm and a laser density of 1-10 J/cm2.

Narciso teaches that photodynamic theapy is also effective during PCTA procedure to limit restenosis of a blood vessel intima subject to a smooth cell proliferation (see abstract). Narciso specifically explains that the use of a photodynamic agent can be during, before or after a PCTA procedure (see col 2, lines 20-35). Narciso also suggests Npe6 to be a suitable photosensitizer for such treatment (see col 7, table 1, under class Phorobides). Narciso teaches the activation wavelength of Npe6 to be

about 660nm and describes suitable dosing. (see table 1). Narciso uses a light dose of 20J/cm2 (see col 8, lines 63-69; col 9, lines 19-34). Narciso teaches that the timing of light delivery following sensitization is about 32 hours and that determination of such parameter is a function of the pharmacokinetics of individual photosensitizers (see col 9, lines 1-55). Since Narcisco teaches the use of photodynamic therapy during a PCTA procedure, all method steps of the instant claims are also inherently disclosed.

Antoshkiw is merely used to show that it is known in the art of balloon catheters to inflate the balloon to totally occlude the blood vessel in order to treat various abnormalities with the blood vessel, such as arteriosclerotic blockage (col. 2, lines 1-8). Therefore, the skilled artisan would have been motivated to totally inflate the balloon catheter as deemed necessary with a reasonable expectation of success in treating arteriosclerotic blood vessels. Therefore, as a result of the blocked blood flow, the centering and proper alignment of the optical fiber is inherent.

Aizawa is merely used to show that the local administration of Npe6 during an intravascular catherization procedure is well described in the art for its therapeutic effects (see col 21, line 60-col 26, line 20). Aizawa also teaches the same doses of Npe6 to produce photosensitizing effects. Aizawa fails to specifically describe the same method during a Percutaneous Transuluminal Coronary Angioplasty procedure (PCTA).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time of invention to substitute the ALA of Nyamekye with another photosensitizer such as Npe6 of Narciso and Aizawa and further improve the clinical outcome and prognosis of patients who undergo angioplasty procedures of Narciso or Nyamekye. One of

ordinary skill in the art would have been motivated to use Npe6 in place of ALA, because as suggested by all cited references any suitable photosensitizer would have provided the same clinical results and are viewed to be art recognized functional equivalents in preventing restenosis secondary to an angioplasty procedure.

Finally, optimizing the laser wavelengths and density is a matter of routine experimentation and as described by Narciso a function of individual sensitizers.

Response to Arguments

Applicant argues that the present invention administers the photosensitive compound a single time, whereas Narciso discloses multiple administrations. Furthermore, new claim 5 uses the transitional phrase "consisting of" to further emphasize that the claimed single photosensitizing compound administration is distinguishable from Narciso.

This is not persuasive because multiple or repeated steps still read on the claimed invention. Examiner views the "consisting of" language to limit the type of photosensitive compound, which is irrelevant here since Narciso teach the same compound. Moreover, the skilled artisan would have been motivated to administer the compound once depending on the efficacy of the treatment regimen.

Applicant argues that the method disclosed in Narciso is distinguishable from the claimed invention because substantially less power, 1 to 10 J/cm^2, is used.

This is not persuasive because Narciso uses a dose of 20 J/cm^2. Therefore, it is obvious to optimize the dosage when the general range is disclosed. Generally, mere optimization of ranges will not support the patentability of subject matter encompassed

by the prior art unless there is evidence indicating such concentration or temperature is critical. "When the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimal or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955); see also *In re Peterson*, 315 F. 3d at 1330, 65 USPQ 2d at 1382 "The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages." MPEP 2114.04.

Applicant argues that Narciso fails to teach or suggest a photodynamic therapy during PTCA procedure. Narciso clearly disclose using photodynamic therapy as an adjunctive therapy to PTCA. Applicant also argues that Narciso fails to teach using a photodynamic agent, but then admits on the record that Narciso uses Npe6 as a photosensitizer. For the record, Narciso clearly discloses Npe6 to be a suitable photosensitizer for such treatment (col. 7, table 1, under class Phorobides).

Applicant argues that Narciso fails to teach inflating a catheter balloon at the prior angioplasty-dilated site during PDT to exert an outward force or pressure on the blood vessel.

This is not persuasive because this limitation is inherent to the PDT procedure, which is known to one of ordinary skill in the art. Nonetheless, Narciso clearly disclose the use of photodynamic therapy during a PCTA procedure. Therefore, the use of a balloon catheter is inherent.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong S. Chong whose telephone number is (571)-272-8513. The examiner can normally be reached on M-F, 9-6.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, SREENI PADMANABHAN can be reached on (571)-272-0629. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

YSC

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER